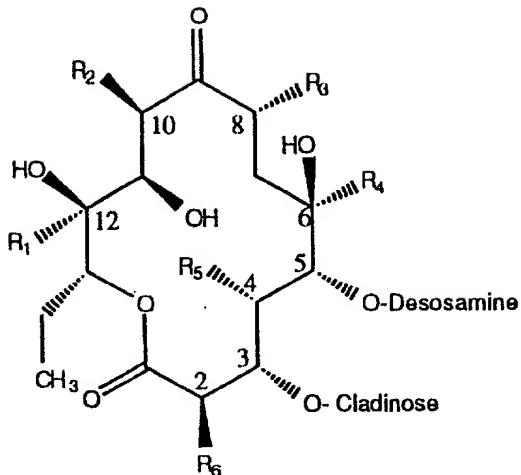


What is claimed is:

1. A compound of the formula:



X

wherein

R₁, R₂, R₃, R₄, R₅, and R₆ are independently selected from Q wherein Q is selected from the group consisting of (a) -H, (b) -Me, (c) -Et, and (d) -OH;

L₁ and L₂ are independently -H or -OH;

L₃ is D-desosamine or -OH; and

L₄ is L-mycarose, L-cladinose or -OH

with the proviso that when R₁-R₅ are -Me, R₆ is other than -H or -Me.

2. The compound of claim 1 wherein Q is selected from the group consisting of (a), (b), and (c) and L₁, L₂, L₃ and L₄ are as defined therein.

3. The compound of claim 1 wherein Q is selected from the group consisting of (a), (b), and (d) and L₁, L₂, L₃ and L₄ are as defined therein.

4. The compound of claim 1 wherein Q is selected from the group consisting of (a), (c), and (d) and L₁, L₂, L₃ and L₄ are as defined therein.

5. The compound of claim 1 wherein Q is selected from the group consisting of (b), (c), and (d) and L₁, L₂, L₃ and L₄ are as defined therein.

6. The compound of claim 1 wherein Q is selected from the group consisting of (a) and (b) and L₁, L₂, L₃ and L₄ are as defined therein.

7. The compound of claim 1 wherein Q is selected from the group consisting of (a) and (c) and L₁, L₂, L₃ and L₄ are as defined therein.

8. The compound of claim 1 wherein Q is selected from the group consisting of (a) and (d) and L₁, L₂, L₃ and L₄ are as defined therein.

9. The compound of claim 1 wherein Q is selected from the group consisting of (b) and (c) and L₁, L₂, L₃ and L₄ are as defined therein.

10. The compound of claim 1 wherein Q is selected from the group consisting of (b) and (d) and L₁, L₂, L₃ and L₄ are as defined therein.

11. The compound of claim 1 wherein Q is selected from the group consisting of (c) and (d) and L₁, L₂, L₃ and L₄ are as defined therein.

12. The compound of claim 1 wherein Q is (a) and L₁, L₂, L₃ and L₄ are as defined therein.

13. The compound of claim 1 wherein Q is (c) and L₁, L₂, L₃ and L₄ are as defined therein.

14. The compound of claim 1 wherein Q is (d) and L₁, L₂, L₃ and L₄ are as defined therein.

15. The compound of claim 1 wherein

- (a) R₆ and R₁ are -H and R₂, R₃, R₄ and R₅ are -Me,
- (b) R₅ and R₁ are -H and R₂, R₃, R₄ and R₆ are -Me,
- (c) R₄ and R₁ are -H and R₂, R₃, R₅ and R₆ are -Me,
- (d) R₃ and R₁ are -H and R₂, R₄, R₅ and R₆ are -Me,
- (e) R₂ and R₁ are -H and R₃, R₄, R₅ and R₆ are -Me,
- (f) R₆ and R₂ are -H and R₁, R₃, R₄ and R₅ are -Me,
- (g) R₅ and R₂ are -H and R₁, R₃, R₄ and R₆ are -Me,
- (h) R₄ and R₂ are -H and R₁, R₃, R₅ and R₆ are -Me,
- (i) R₃ and R₂ are -H and R₁, R₄, R₅ and R₆ are -Me,
- (j) R₆ and R₃ are -H and R₁, R₂, R₄ and R₅ are -Me,
- (k) R₅ and R₃ are -H and R₁, R₂, R₄ and R₆ are -Me,
- (l) R₄ and R₃ are -H and R₁, R₂, R₅ and R₆ are -Me,

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- (m) R₆ and R₄ are -H and R₁, R₂, R₃ and R₅ are -Me,
- (n) R₅ and R₄ are -H and R₁, R₂, R₃ and R₆ are -Me,
- (o) R₆ and R₅ are -H and R₁, R₂, R₃ and R₄ are -Me, and L₁, L₂, L₃ and L₄ are as defined therein.

16. The compound of claim 15 wherein (a)-(o) are as defined therein, L₁ and L₂ are -OH, L₃ is D-desosamine and L₄ is L-cladinose.

17. The compound of claim 1 wherein

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- (a) R₆, R₂ and R₁ are -H and R₃, R₄ and R₅ are -Me,
- (b) R₅, R₂ and R₁ are -H and R₃, R₄ and R₆ are -Me,
- (c) R₄, R₂ and R₁ are -H and R₃, R₅ and R₆ are -Me,
- (d) R₃, R₂ and R₁ are -H and R₄, R₅ and R₆ are -Me,
- (e) R₆, R₃ and R₁ are -H and R₂, R₄ and R₅ are -Me,
- (f) R₅, R₃ and R₁ are -H and R₂, R₄ and R₆ are -Me,
- (g) R₄, R₃ and R₁ are -H and R₂, R₅ and R₆ are -Me,
- (h) R₆, R₄ and R₁ are -H and R₂, R₃ and R₅ are -Me,
- (i) R₅, R₄ and R₁ are -H and R₂, R₃ and R₆ are -Me,
- (j) R₆, R₅ and R₁ are -H and R₂, R₃ and R₄ are -Me,
- (k) R₆, R₃ and R₂ are -H and R₁, R₄ and R₅ are -Me,
- (l) R₅, R₃ and R₂ are -H and R₁, R₄ and R₆ are -Me,
- (m) R₄, R₃ and R₂ are -H and R₁, R₅ and R₆ are -Me,
- (n) R₆, R₄ and R₂ are -H and R₁, R₃ and R₅ are -Me,
- (o) R₅, R₄ and R₂ are -H and R₁, R₃ and R₆ are -Me,
- (p) R₆, R₅ and R₂ are -H and R₁, R₃ and R₄ are -Me,
- (q) R₆, R₄ and R₃ are -H and R₁, R₂ and R₅ are -Me,
- (r) R₅, R₄ and R₃ are -H and R₁, R₂ and R₆ are -Me,
- (s) R₆, R₅ and R₃ are -H and R₁, R₂ and R₄ are -Me, or
- (t) R₆, R₅ and R₄ are -H and R₁, R₂ and R₃ are -Me, and L₁, L₂, L₃ and L₄ are as defined therein.

18. The compound of claim 17 wherein (a)-(t) are as defined therein, L₁ and L₂ are -OH, L₃ is D-desosamine and L₄ is L-cladinose.

19. The compound of claim 1 wherein

- (a) R₆, R₃, R₂ and R₁ are -H and R₅, and R₄ are -Me,
- (b) R₅, R₃, R₂ and R₁ are -H and R₆, and R₄ are -Me,
- (c) R₄, R₃, R₂ and R₁ are -H and R₅, and R₆ are -Me,

20. The compound of claim 19 wherein (a)-(n) are as defined therein, L₁ and L₂ are -OH, L₃ is D-desosamine and L₄ is L-cladinose.

21. The compound of claim 1 wherein

- (a) R₅, R₄, R₃, R₂ and R₁ are -H and R₆ is -Me,
- (b) R₆, R₄, R₃, R₂ and R₁ are -H and R₅ is -Me,
- (c) R₆, R₅, R₃, R₂ and R₁ are -H and R₄ is -Me,
- (d) R₆, R₅, R₄, R₂ and R₁ are -H and R₃ is -Me,
- (e) R₆, R₅, R₄, R₃ and R₁ are -H and R₂ is -Me, or
- (f) R₆, R₅, R₄, R₃ and R₂ are -H and R₁ is -Me, and

L_1 , L_2 , L_3 and L_4 are as defined therein.

22. The compound of claim 21 wherein (a)-(f) are as defined therein, L₁ and L₂ are -OH, L₃ is D-desosamine and L₄ is L-cladinose.

23. The compound of claim 1 wherein R₁, R₂, R₃, R₄, R₅ and R₆ are -H and L₁, L₂, L₃ and L₄ are as defined therein.

24. The compound of claim 23 wherein R₁, R₂, R₃, R₄, R₅ and R₆ are as defined therein, L₁ and L₂ are -OH, L₃ is D-desosamine and L₄ is L-cladinose.

25. The compound of claim 1 selected from the group consisting of 6,10-didesmethyl-6-ethylerythromycin A; 10,12-didesmethyl-12-deoxy-12-ethylerythromycin A; 10,12-didesmethyl-12-deoxy-10-hydroxyerythromycin A; 6,10,12-tridesmethyl-6,12-diethylerythromycin A, and 6,10,12-tridesmethyl-6-deoxy-6,12-diethylerythromycin A.

26. The compound of claim 1 selected from the group consisting of 10-desmethylerythronolide B, 10-desmethyl-6-deoxyerythronolide B, 12-desmethylerythronolide B, 12-desmethyl-6-deoxyerythronolide B, 12-desmethyl-12-ethylerythronolide B, 6-desmethyl-6-deoxy-6-ethylerythronolide B, 10-desmethylerythromycin A, 10-desmethyl-12-deoxyerythromycin A, 10-desmethyl-6,12-dideoxyerythromycin A, 12-desmethylerythromycin A, 12-desmethyl-12-deoxyerythromycin A, 12-desmethyl-6,12-dideoxyerythromycin A, 6-desmethyl-6-ethylerythromycin A, 12-desmethyl-12-ethylerythromycin A, 12-desmethyl-12-deoxy-12-ethylerythromycin A, 10-desmethyl-10-hydroxyerythromycin A, 12-desmethyl-12-epihydroxyerythromycin A, 10,12-didesmethylerythromycin A, 10,12-didesmethyl-12-deoxyerythromycin A, and 10,12-didesmethyl-6,12-dideoxyerythromycin A.

27. The compound of claim 1 selected from the group consisting of 10-desmethylerythronolide B, 10-desmethyl-6-deoxyerythronolide B, 12-desmethylerythronolide B, 12-desmethyl-6-deoxyerythronolide B, 10-desmethylerythromycin A, 10-desmethyl-12-deoxyerythromycin A, 10-desmethyl-6,12-dideoxyerythromycin A, 12-desmethylerythromycin A, 12-desmethyl-12-deoxyerythromycin A, 12-desmethyl-6,12-dideoxyerythromycin A, 10,12-didesmethylerythromycin A, 10,12-didesmethyl-12-deoxyerythromycin A, and 10,12-didesmethyl-6,12-dideoxyerythromycin A.

28. A compound selected from the group consisting of 10-desmethylerythromycin A, 10-desmethyl-12-deoxyerythromycin A, and 12-desmethyl-12-deoxyerythromycin A.

29. An isolated polynucleotide sequence or fragment thereof which encodes an enzymatically active acyltransferase domain from a polyketide-producing microorganism selected from the group consisting of *Streptomyces hygroscopicus*, *Streptomyces venezuelae*, and *Streptomyces caelestis*.

30. The polynucleotide of Claim 29 selected from the group consisting of SEQ ID NO:1, SEQ ID NO:2, SEQ ID NO:29 and SEQ ID NO:30.

31. The polynucleotide of Claim 29 wherein said acyltransferase domain is selected from the group consisting of SEQ ID NO:31, SEQ ID NO:32, SEQ ID NO:33 and SEQ ID NO:34.

32. A vector comprising a polynucleotide sequence or fragment thereof which encodes an enzymatically active acyltransferase domain from *Streptomyces*.

33. The vector of Claim 32 wherein said *Streptomyces* is selected from the group consisting of *Streptomyces hygroscopicus*, *Streptomyces venezuelae*, and *Streptomyces caelestis*.

34. The vector of Claim 32 which is pCS5.

35. The vector of Claim 32 wherein said polynucleotide is selected from the group consisting of SEQ ID NO:1, SEQ ID NO:2, SEQ ID NO:29 and SEQ ID NO:30.

36. The vector of Claim 32 wherein said acyltransferase domain is selected from the group consisting of SEQ ID NO:31, SEQ ID NO:32, SEQ ID NO:33 and SEQ ID NO:34.

37. A vector selected from the group consisting of pUC18/LigAT2, pEryAT1/LigAT2, pEryAT2/LigAT2, pUC18/venAT, pEryAT1/venAT, pUC19/rapAT14, pEryAT1/rapAT14, pEryAT2/rapAT14, pUC/5'-flank/ethAT, pUC/ethAT/C-6, pEAT4, pUC18/NidAT6, and pEryAT2/NidAT6.

38. A host cell transformed with the vector of Claim 32.

39. The host cell of Claim 38 wherein said cell is a bacterial cell.

40. The host cell of Claim 39 wherein said bacterial cell is selected from the group consisting of *E. coli* and *Bacillus* species.

41. The host cell of Claim 40 wherein said cell is a polyketide-producing microorganism.

42. The host cell of Claim 41 wherein said polyketide-producing microorganism is selected from the group consisting of *Saccharopolyspora* species, *Nocardia* species, *Micromonospora* species, *Arthrobacter* species, *Streptomyces* species, *Actinomadura* species, and *Dactylosporangium* species.

43. The host cell of Claim 42 wherein said polyketide-producing microorganism is selected from the group consisting of *Saccharopolyspora hirsuta*, *Micromonospora rosaria*, *Micromonospora megalomicea*, *Streptomyces antibioticus*, *Streptomyces mycarofaciens*, *Streptomyces avermitilis*, *Streptomyces hygroscopicus*, *Streptomyces caelestis*, *Streptomyces tsukubaensis*, *Streptomyces fradiae*, *Streptomyces platensis*, *Streptomyces violaceoniger*, *Streptomyces ambofaciens*, *Streptomyces griseoplanus*, and *Streptomyces venezuelae*.

44. The host cell of Claim 42 wherein said polyketide-producing microorganism is selected from the group consisting of *Saccharopolyspora* species and *Streptomyces* species.

45. The host cell of Claim 44 wherein said polyketide-producing microorganism is *Saccharopolyspora erythraea*.

46. The host cell of Claim 44 wherein said polyketide-producing microorganism is selected from the group consisting of *Streptomyces hygroscopicus*, *Streptomyces venezuelae*, and *Streptomyces caelstis*.

47. A method for altering the substrate specificity of a polyketide synthase in a first polyketide-producing microorganism comprising the steps of:

(a) isolating a first and second genomic DNA segment, each comprising a polyketide synthase wherein said first genomic DNA segment is from said first polyketide-producing microorganism and said second genomic DNA segment is from said first polyketide-producing microorganism or a second polyketide-producing microorganism;

(b) identifying one or more discrete fragments of said first genomic DNA segment, each of which encodes an acyltransferase domain;

(c) identifying one or more discrete fragments of said second genomic DNA segment, each of which encodes a related domain to said acyltransferase domain of said first genomic DNA segment; and

(d) transforming a cell of said first polyketide-producing microorganism with one or more of said fragments from step (c) under conditions suitable for the occurrence of a homologous recombination event, leading to the replacement of one or more of said fragments from said first genomic DNA segment with one or more of said fragments from step (c).

48. The method of Claim 47 wherein said first polyketide-producing microorganism is *Saccharopolyspora erythraea*.

49. The method of Claim 47 wherein said second polyketide-producing microorganism is *Streptomyces*.

50. The method of Claim 49 wherein said *Streptomyces* is selected from the group consisting of *Streptomyces antibioticus*, *Streptomyces mycarofaciens*, *Streptomyces avermitilis*, *Streptomyces hygroscopicus*, *Streptomyces caelstis*, *Streptomyces tsukubaensis*, *Streptomyces fradiae*, *Streptomyces platensis*, *Streptomyces violaceoniger*, *Streptomyces ambofaciens*, and *Streptomyces venezuelae*.

51. The method of Claim 50 wherein said *Streptomyces* is selected from the group consisting of *Streptomyces caelensis*, *Streptomyces hygroscopicus*, and *Streptomyces venezuelae*.

52. The method of Claim 47 wherein said first polyketide-producing microorganism is *Streptomyces*.

53. The method of Claim 52 wherein said *Streptomyces* is selected from the group consisting of *Streptomyces antibioticus*, *Streptomyces mycarofaciens*, *Streptomyces avermitilis*, *Streptomyces hygroscopicus*, *Streptomyces caelensis*, *Streptomyces tsukubaensis*, *Streptomyces fradiae*, *Streptomyces platensis*, *Streptomyces violaceoniger*, *Streptomyces ambofaciens*, and *Streptomyces venezuelae*.

54. The method of Claim 53 wherein said *Streptomyces* is selected from the group consisting of *Streptomyces caelensis*, *Streptomyces hygroscopicus*, and *Streptomyces venezuelae*.

55. The method of Claim 47 wherein said second polyketide-producing microorganism is *Saccharopolyspora erythraea*.

56. The method of Claim 47 wherein said related domain is selected from the group consisting of SEQ ID NO:31, SEQ ID NO:32, SEQ ID NO:33 and SEQ ID NO:34.